Notice of Allowability	Application No.	Applicant(s)	
	10/527,762	DUFFY ET AL.	
	Examiner	Art Unit	
	Joseph Kosack	1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to *Response to Restriction filed 09 March 2007*.

2. ☒ The allowed claim(s) is/are *1-3,5-7,9 and 11-13*.

3. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
   a) ☐ All b) ☐ Some* c) ☐ None of the:
      1. ☐ Certified copies of the priority documents have been received.
      2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
      3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

   * Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

4. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.

5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
   (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
      1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.
   (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.

   Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).

6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☒ Notice of References Cited (PTO-892)
2. ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
3. ☒ Information Disclosure Statements (PTO/SB/08), Paper No./Mail Date 12/11/06
4. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
5. ☐ Notice of Informal Patent Application
6. ☐ Interview Summary (PTO-413), Paper No./Mail Date _____ .
7. ☒ Examiner's Amendment/Comment
8. ☒ Examiner's Statement of Reasons for Allowance
9. ☐ Other _____.

DETAILED ACTION

Claims 1-15 are pending in the instant application.

Election/Restrictions

Applicant's election of Group I along with an election of species with traverse filed March 09, 2007 has been noted. The traversal has been found to be persuasive and the lack of unity requirement will be modified as stated below.

Group I, claim(s) 1-13 (in part), drawn to compounds and uses of compounds of Formula I where X is NR^4, m is 0, and n is 3.

Group II, claim(s) 1-13 (in part), drawn to compounds and uses of compounds of Formula I where X is NR^4, m is 0, and n is 2.

Group III, claim(s) 1-13 (in part), drawn to compounds and uses of compounds of Formula I where X is NR^4, m is 1, and n is 2.

Group IV, claim(s) 1-13 (in part), drawn to compounds and uses of compounds of Formula I where X is NR^4, m is 1, and n is 1.

Group V, claim(s) 1-13 (in part), drawn to compounds and uses of compounds of Formula I where X is NR^4, m is 2, and n is 1.

Group VI, claim(s) 1-13 (in part), drawn to compounds and uses of compounds of Formula I where X is NR^4, m is 2, and n is 0.

Group VII, claim(s) 1-13 (in part), drawn to compounds and uses of compounds of Formula I where X is NR^4, m is 3, and n is 0.

Group VIII, claim(s) 1-13 (in part), drawn to compounds and uses of compounds of Formula I where X is CR^5R^6, m is 0, and n is 3.

Group IX, claim(s) 1-13 (in part), drawn to compounds and uses of compounds of Formula I where X is CR^5R^6, m is 0, and n is 2.

Group X, claim(s) 1-13 (in part), drawn to compounds and uses of compounds of Formula I where X is CR^5R^6, m is 1, and n is 2.

Group XI, claim(s) 1-13 (in part), drawn to compounds and uses of compounds of Formula I where X is CR^5R^6, m is 1, and n is 1.

Group XII, claim(s) 1-13 (in part), drawn to compounds and uses of compounds of Formula I where X is CR^5R^6, m is 2, and n is 1.

Group XIII, claim(s) 1-13 (in part), drawn to compounds and uses of compounds of Formula I where X is CR^5R^6, m is 2, and n is 0.

Group XIV, claim(s) 1-13 (in part), drawn to compounds and uses of compounds of Formula I where X is CR^5R^6, m is 3, and n is 0.

Group XV, claim(s) 14-15, drawn to additional methods of using compound of Formula I.

The inventions listed as Groups I-XV do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: they have differing core structures and therefore contain differing special technical features.

During a telephone conversation with Richard C. Billups on June 13, 2007 a provisional election was made without traverse to prosecute the invention of Group I, claims 1-13 (in part). Affirmation of this election must be made by applicant in replying to this Office action. Claims 1-13 (in part) and 14-15 withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Priority

The claim to priority as a 371 filing of PCT/US03/28033 filed September 8, 2003 which claims priority to 60/410,145 is granted in the instant application.

Information Disclosure Statement

The Information Disclosure Statement filed December 11, 2006 has been considered fully by the Examiner.

EXAMINER'S AMENDMENT

An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Richard C. Billups on June 13, 2007.

The application has been amended as follows:

See attached claims.

Reasons for Allowance

The closest prior art is that of Fujita et al. (*Bioorganic and Medicinal Chemistry Letters, 2002*, 1897-1900). Fujita et al. teach compounds that have the nitrogen in a different position of the 6-membered ring than the compounds of the instant claims. Since the ring is not an aryl ring which would allow for bioisosteric replacement, Fujita et al. do not anticipate or suggest the instant invention.

Conclusion

Claims 1-3, 5-7, 9, and 11-13 are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph Kosack whose telephone number is (571)-272-5575. The examiner can normally be reached on M-F 6:30 A.M. until 4:00 P.M. The examiner has every other Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph McKane can be reached on (571)-272-0699. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Joseph R Kosack

Joseph Kosack
Patent Examiner
Art Unit 1626

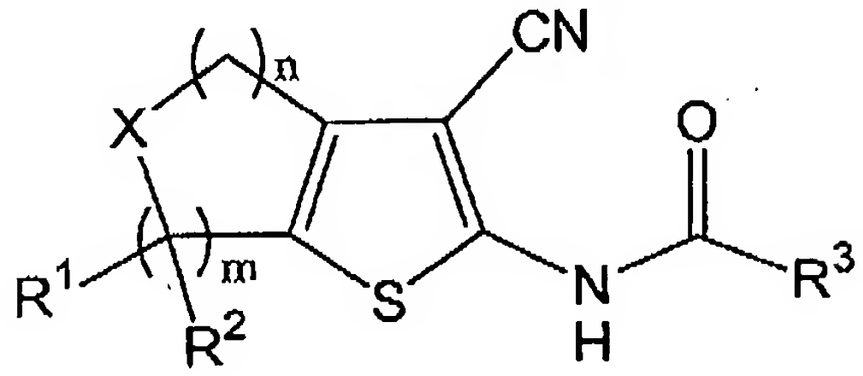
REBECCA ANDERSON
PATENT EXAMINER

Joseph K. McKane
Supervisory Patent Examiner
Art Unit 1626

EXAMINER'S AMENDMENT

WHAT IS CLAIMED IS:

1. A compound represented by formula I:



or a pharmaceutically acceptable salt or solvate thereof wherein:

X is NR^4;

R^1 is selected from the group consisting of: H, C_{1-10}alkyl, C_{3-7}cycloalkyl and Aryl, said alkyl, cycloalkyl and Aryl being optionally substituted with 1-4 substituents independently selected from R^{13};

R^2 is selected from the group consisting of: R^1 as defined above, $-C(O)_2R^7$ and $-CONR^7R^8$;

m is 0;

n is 3;

R^3 is selected from the group consisting of: C_{1-10}alkyl, C_{3-7}cycloalkyl and Aryl, said alkyl, cycloalkyl and Aryl being optionally substituted with 1-4 substituents selected from R^{13}, such that when R^3 represents C_{1-10} alkyl substituted with one R^{13} group, and R^{13} represents halo, R^1, R^2, R^5 and R^6 do not represent C_{1-3}alkyl;

R^4 is selected from the group consisting of: C_{3-10} alkyl, C_{3-7} cycloalkyl, Aryl, HAR, Hetcy, $C(O)C_{5-10}$ alkyl, $C(O)C_{3-7}$ cycloalkyl, C(O)-Aryl, C(O)-HAR, C(O)-Hetcy, $CONR^9R^{10}$, CO_2R^9 and SO_2R^9, the alkyl, cycloalkyl, Aryl, HAR and Hetcy groups and portions being optionally substituted with 1-4 substituents selected from R^{13};

one of $R^5$and R^6 is selected from the group consisting of $NR^{11}R^{12}$, $NR^{11}COR^{12}$, $NR^{11}CO_2R^{12}$ and $NR^{11}S(O)_2R^{12}$, and the other represents R^1, HAR, Hetcy or OR^{11}, said HAR and Hetcy being optionally substituted with 1-4 substituents selected from R^{13},

R^7, R^{10} and R^{11} are selected from the group consisting of: R^1 as defined above, HAR and Hetcy, said HAR and Hetcy being optionally substituted with 1-4 substituents selected from R^{13};

R^8, R^9 and R^{12} are selected from the group consisting of: C_{1-10}alkyl, C_{3-7}cycloalkyl, Aryl, HAR and Hetcy, said alkyl, cycloalkyl, Aryl, HAR and Hetcy being optionally substituted with 1-4 substituents selected from R^{13};

or alternatively, R^7, R^8, R^9 and R^{10} are as defined above, and R^{11} and R^{12} are taken together with the atoms to which they are attached along with any intervening atoms and represent a 5-8 membered ring optionally containing 1-2 heteroatoms selected from O, S and N, and optionally substituted with 1-4 substituents selected from R^{13};

each R^{13} is selected from the group consisting of: halo, $NR^{14}R^{15}$, C_{1-4}alkyl, C_{3-7}-cycloalkyl, Aryl, HAR, Hetcy, CF_3, OCF_3, OR^{15}, NO_2, $S(O)_xR^{14}$, SR^{14}, $S(O)_xNR^{14}R^{15}$, $O(CR^{16}R^{17})_yNR^{14}R^{15}$, $C(O)R^{14}$, CO_2R^{15}, $CO_2(CR^{16}R^{17})_yCONR^{14}R^{15}$, $OC(O)R^{14}$, CN, $C(O)NR^{14}R^{15}$, $NR^{15}C(O)R^{14}$, $NR^{15}C(O)OR^{14}$, $NR^{15}C(O)NR^{16}R^{14}$ and $CR^{15}(N\text{-}OR^{14})$, wherein x is 1 or 2, and y is an integer from 1-4,

said alkyl, cycloalkyl, Aryl, HAR and Hetcy being optionally substituted with 1-4 substituents selected from R^{18};

R^{14}, R^{15}, R^{16} and R^{17} are independently selected from the group consisting of: H, C_{1-10}alkyl, C_{3-7}cycloalkyl, Aryl and Ar-C_{1-10}alkyl;

and each R^{18} is independently selected from the group consisting of: halogen, CN, C_{1-4}alkyl, OH, CF_3, Aryl, Aryloxy, CO_2H and CO_2C_{1-4} alkyl, said Aryl and the Aryl portion of Aryloxy being optionally substituted with up to 4 halo groups, and up to 2 C_{1-4} alkyl, OH, CF_3 or CN groups.

2. A compound in accordance with claim 1 wherein R^1 is selected from the group consisting of: H, C_{1-10}alkyl, C_{3-6} cycloalkyl and phenyl, said alkyl and phenyl being optionally substituted with 1-3 substituents selected from R^{13}.

3. A compound in accordance with claim 1 wherein R^2 is H.

4. (Cancelled)

5. A compound in accordance with claim 1 wherein R^3 is C_{3-10} alkyl optionally substituted with 1-4 substituents selected from R^{13}, such that when R^3 is substituted with one R^{13} group, and R^{13} represents halo, R^1, R^2, R^5 and R^6 do not represent C_{1-3}alkyl.

6. A compound in accordance with claim 5 wherein R^3 represents C_{3-5} alkyl, optionally substituted with 1-4 R^{13} groups.

7. A compound in accordance with claim 1 wherein R^4 is selected from the group consisting of: C_{5-10} alkyl, C_{3-6} cycloalkyl, phenyl, HAR, Hetcy, $C(O)C_{5-10}$alkyl, $C(O)C_{3-6}$ cycloalkyl and CO_2R^9, the alkyl, cycloalkyl and, Aryl groups and portions, phenyl, HAR and Hetcy being optionally substituted with 1-4 substituents selected from R^{13}, and R^9 representing C_{1-10}alkyl, C_{3-7}cycloalkyl, Aryl, HAR or Hetcy, said alkyl, cycloalkyl, Aryl groups and portions, HAR and Hetcy being optionally substituted with 1-4 R^{13} groups.

8. (Cancelled)

9. A compound in accordance with claim 1 wherein R^{13} is selected from the group consisting of: halo, C_{1-4}alkyl, C_{3-7}cycloalkyl, Aryl, HAR, Hetcy, and OR^{15} wherein R^{15} is H,

said alkyl, cycloalkyl, Aryl, HAR and Hetcy being optionally substituted with 1-4 substituents selected from R^{18} and

R^{18} is halo, C_{1-4}alkyl, Aryl or CO_2C_{1-4} alkyl.

10. (Cancelled)

11. A compound in accordance with claim 1 selected from the group consisting of: tert-butyl 3-cyano-2-[(2-ethylbutanoyl)amino]-5,6-dihydrothieno[2,3-b]pyridine-7(4H)-carboxylate; N-(3-cyano-7-isobutyl-4,5,6,7-tetrahydrothieno[2,3-b]pyridin-2-yl)-2-ethylbutanamide; and N-(3-cyano-7-isopropyl-4,5,6,7-tetrahydrothieno[2,3-b]pyridin-2-yl)-2-ethylbutanamide.

12. A pharmaceutical composition which is comprised of a compound in accordance with claim 1 in combination with a pharmaceutically acceptable carrier.

13. A method of treating type 2 diabetes mellitus in a mammalian patient in need of such treatment, comprising administering to said patient a compound in accordance with claim 1 in an amount that is effective to treat type 2 diabetes mellitus.

14. (Cancelled)

15. (Cancelled)

MERCK

Merck & Co., Inc.
P.O. Box 2000
Rahway, NJ 07065

Patent Department

REQUESTED JK 6/15/07

Facsimile Cover Sheet

TODAY'S DATE: June 14. 2007

PLEASE DELIVER THE FOLLOWING MESSAGE TO:

Fax No.: 571-273-5575

Attention: Examiner Kosack

THIS MESSAGE IS FROM:

Name: Richard C. Billups

Phone No.: (732)594-4683 Mail Location: RY60-30

Fax No.: (732)594-4720

Appl. No.: 10/527,762
Filing Date: March 11, 2003
Docket No.: 21163P
For: SUBSTITUTED BICYCLIC THIOPENE DERIVATIVES, COMPOSITIONS CONTAINING SUCH COMPOUNDS AND METHODS OF USE

Examiner Kosack,

Attached please find a new clean copy of the claims, without renumbering, as per our discussion earlier today. If you require anything further to complete processing, please telephone me as soon as possible. Thank you again for your assistance.

Respectfully submitted,

Richard C. Billups
Reg. No. 31,916

NUMBER OF PAGES BEING TRANSMITTED (INCLUDING COVER): 5

Documents sent: Proposed claims (clean copy)

IF YOU DO NOT RECEIVE ALL OF THE PAGES, PLEASE CALL (732) 594-8554

CERTIFICATION OF FACSIMILE TRANSMISSION

I hereby certify that this paper is being facsimile transmitted to the United States Patent and Trademark Office on the date shown below

KAREN ANN DROST
Type or print name of person signing certification

Signature *Date* 12-14-07

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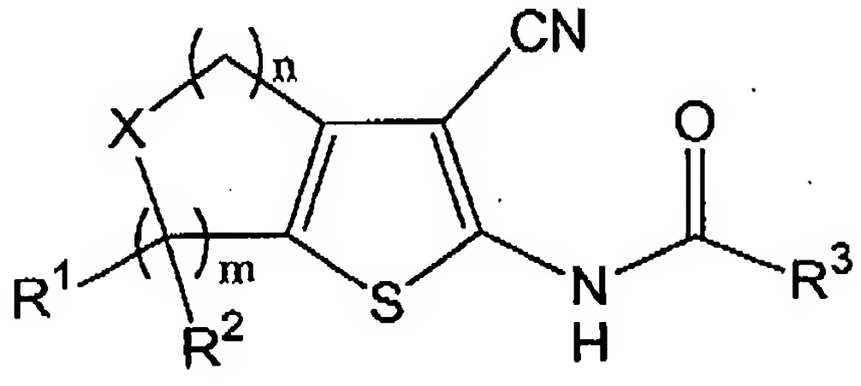
WHAT IS CLAIMED IS:

1. A compound represented by formula I:



or a pharmaceutically acceptable salt or solvate thereof wherein:

X is NR^4;

R^1 is selected from the group consisting of: H, C_{1-10}alkyl, C_{3-7}cycloalkyl and Aryl, said alkyl, cycloalkyl and Aryl being optionally substituted with 1-4 substituents independently selected from R^{13};

R^2 is selected from the group consisting of: R^1 as defined above, $-C(O)_2R^7$ and $-CONR^7R^8$;

m is 0;

n is 3;

R^3 is selected from the group consisting of: C_{1-10}alkyl, C_{3-7}cycloalkyl and Aryl, said alkyl, cycloalkyl and Aryl being optionally substituted with 1-4 substituents selected from R^{13}, such that when R^3 represents C_{1-10} alkyl substituted with one R^{13} group, and R^{13} represents halo, R^1, R^2, R^5 and R^6 do not represent C_{1-3}alkyl;

R^4 is selected from the group consisting of: C_{3-10} alkyl, C_{3-7} cycloalkyl, Aryl, HAR, Hetcy, $C(O)C_{5-10}$ alkyl, $C(O)C_{3-7}$ cycloalkyl, C(O)-Aryl, C(O)-HAR, C(O)-Hetcy, $CONR^9R^{10}$, CO_2R^9 and SO_2R^9, the alkyl, cycloalkyl, Aryl, HAR and Hetcy groups and portions being optionally substituted with 1-4 substituents selected from R^{13};

one of $R^5$and R^6 is selected from the group consisting of $NR^{11}R^{12}$, $NR^{11}COR^{12}$, $NR^{11}CO_2R^{12}$ and $NR^{11}S(O)_2R^{12}$, and the other represents R^1, HAR, Hetcy or OR^{11}, said HAR and Hetcy being optionally substituted with 1-4 substituents selected from R^{13},

R^7, R^{10} and R^{11} are selected from the group consisting of: R^1 as defined above, HAR and Hetcy, said HAR and Hetcy being optionally substituted with 1-4 substituents selected from R^{13};

R^8, R^9 and R^{12} are selected from the group consisting of: C_{1-10}alkyl, C_{3-7}cycloalkyl, Aryl, HAR and Hetcy, said alkyl, cycloalkyl, Aryl, HAR and Hetcy being optionally substituted with 1-4 substituents selected from R^{13};

or alternatively, R^7, R^8, R^9 and R^{10} are as defined above, and R^{11} and R^{12} are taken together with the atoms to which they are attached along with any intervening atoms and represent a 5-8 membered ring optionally containing 1-2 heteroatoms selected from O, S and N, and optionally substituted with 1-4 substituents selected from R^{13};

each R^{13} is selected from the group consisting of: halo, $NR^{14}R^{15}$, C_{1-4}alkyl, C_{3-7}-cycloalkyl, Aryl, HAR, Hetcy, CF_3, OCF_3, OR^{15}, NO_2, $S(O)_XR^{14}$, SR^{14}, $S(O)_XNR^{14}R^{15}$, $O(CR^{16}R^{17})_yNR^{14}R^{15}$, $C(O)R^{14}$, CO_2R^{15}, $CO_2(CR^{16}R^{17})_yCONR^{14}R^{15}$, $OC(O)R^{14}$, CN, $C(O)NR^{14}R^{15}$, $NR^{15}C(O)R^{14}$, $NR^{15}C(O)OR^{14}$, $NR^{15}C(O)NR^{16}R^{14}$ and $CR^{15}(N\text{-}OR^{14})$, wherein x is 1 or 2, and y is an integer from 1-4,

said alkyl, cycloalkyl, Aryl, HAR and Hetcy being optionally substituted with 1-4 substituents selected from R^{18};

R^{14}, R^{15}, R^{16} and R^{17} are independently selected from the group consisting of: H, C_{1-10}alkyl, C_{3-7}cycloalkyl, Aryl and Ar-C_{1-10}alkyl;

and each R^{18} is independently selected from the group consisting of: halogen, CN, C_{1-4}alkyl, OH, CF_3, Aryl, Aryloxy, CO_2H and CO_2C_{1-4} alkyl, said Aryl and the Aryl portion of Aryloxy being optionally substituted with up to 4 halo groups, and up to 2 C_{1-4} alkyl, OH, CF_3 or CN groups.

2. A compound in accordance with claim 1 wherein R^1 is selected from the group consisting of: H, C_{1-10}alkyl, C_{3-6} cycloalkyl and phenyl, said alkyl and phenyl being optionally substituted with 1-3 substituents selected from R^{13}.

3. A compound in accordance with claim 1 wherein R^2 is H.

4. (Cancelled)

5. A compound in accordance with claim 1 wherein R^3 is C_{3-10} alkyl optionally substituted with 1-4 substituents selected from R^{13}, such that when R^3 is substituted with one R^{13} group, and R^{13} represents halo, R^1, R^2, R^5 and R^6 do not represent C_{1-3}alkyl.

6. A compound in accordance with claim 5 wherein R^3 represents C_{3-5} alkyl, optionally substituted with 1-4 R^{13} groups.

7. A compound in accordance with claim 1 wherein R^4 is selected from the group consisting of: C_{5-10} alkyl, C_{3-6} cycloalkyl, phenyl, HAR, Hetcy, $C(O)C_{5-10}$alkyl, $C(O)C_{3-6}$ cycloalkyl and CO_2R^9, the alkyl, cycloalkyl and, Aryl groups and portions, phenyl, HAR and Hetcy being optionally substituted with 1-4 substituents selected from R^{13}, and R^9 representing C_{1-10}alkyl, C_{3-7}cycloalkyl, Aryl, HAR or Hetcy, said alkyl, cycloalkyl, Aryl groups and portions, HAR and Hetcy being optionally substituted with 1-4 R^{13} groups.

8. (Cancelled)

9. A compound in accordance with claim 1 wherein R^{13} is selected from the group consisting of: halo, C_{1-4}alkyl, C_{3-7}cycloalkyl, Aryl, HAR, Hetcy, and OR^{15} wherein R^{15} is H,

said alkyl, cycloalkyl, Aryl, HAR and Hetcy being optionally substituted with 1-4 substituents selected from R^{18} and

R^{18} is halo, C_{1-4}alkyl, Aryl or CO_2C_{1-4} alkyl.

10. (Cancelled)

11. A compound in accordance with claim 1 selected from the group consisting of: tert-butyl 3-cyano-2-[(2-ethylbutanoyl)amino]-5,6-dihydrothieno[2,3-b]pyridine-7(4H)-carboxylate; N-(3-cyano-7-isobutyl-4,5,6,7-tetrahydrothieno[2,3-b]pyridin-2-yl)-2-ethylbutanamide; and N-(3-cyano-7-isopropyl-4,5,6,7-tetrahydrothieno[2,3-b]pyridin-2-yl)-2-ethylbutanamide.

12. A pharmaceutical composition which is comprised of a compound in accordance with claim 1 in combination with a pharmaceutically acceptable carrier.

13. A method of treating type 2 diabetes mellitus in a mammalian patient in need of such treatment, comprising administering to said patient a compound in accordance with claim 1 in an amount that is effective to treat type 2 diabetes mellitus.

14. (Cancelled)

15. (Cancelled)

MERCK

Merck & Co., Inc.
P.O. Box 2000
Rahway, NJ 07065

Patent Department

REQUESTED
JK 6/15/07

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TODAY'S DATE: June 14, 2007

PLEASE DELIVER THE FOLLOWING MESSAGE TO:

Fax No.: 571-273-5575

Attention: Examiner Kosack

THIS MESSAGE IS FROM:

Name: Richard C. Billups

Phone No.: (732)594-4683 Mail Location: RY60-30

Fax No.: (732)594-4720

Appl. No.: 10/527,762
Filing Date: March 11, 2003
Docket No.: 21163P
For: SUBSTITUTED BICYCLIC THIOPENE DERIVATIVES, COMPOSITIONS CONTAINING SUCH COMPOUNDS AND METHODS OF USE

Examiner Kosack,

Enclosed please find the marked up copy of the claims, as per our discussion this afternoon. If you require anything further to complete processing, please call me as soon as possible. Thank you again for your assistance.

Respectfully submitted,

Richard C. Billups
Reg. No. 31,916

NUMBER OF PAGES BEING TRANSMITTED (INCLUDING COVER): 8

Documents sent: Proposed claims (clean copy), proposed claims (marked up version)

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KAREN ANN DROST
Type or print name of person signing certification

Signature 6-14-07 *Date*

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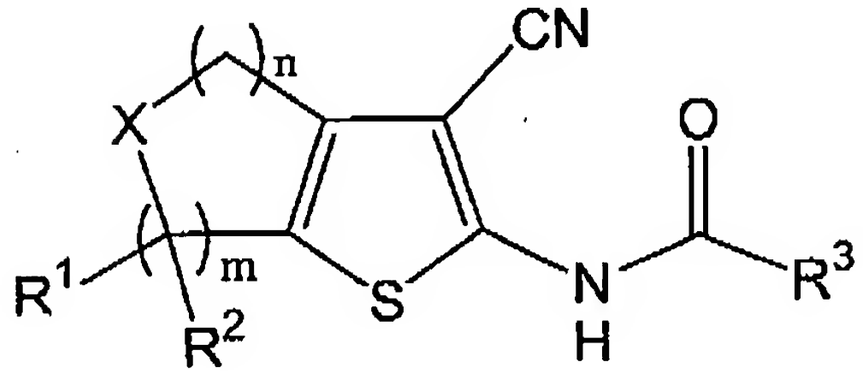
1. (Amended) A compound represented by formula I:



or a pharmaceutically acceptable salt or solvate thereof wherein:

X is NR^4 ~~or CR^5R^6~~;

R^1 is selected from the group consisting of: H, C_{1-10}alkyl, C_{3-7}cycloalkyl and Aryl, said alkyl, cycloalkyl and Aryl being optionally substituted with 1-4 substituents independently selected from R^{13};

R^2 is selected from the group consisting of: R^1 as defined above, $-C(O)_2R^7$ and $-CONR^7R^8$;

~~m and n are selected from 0, 1, 2 and 3, such that the sum of m and n is 2 or 3, and when m is greater than 1, no more than one R^1 and no more than one R^2 can be other than H;~~

m is 0;

n is 3;

R^3 is selected from the group consisting of: C_{1-10}alkyl, C_{3-7}cycloalkyl and Aryl, said alkyl, cycloalkyl and Aryl being optionally substituted with 1-4 substituents selected from R^{13}, such that when R^3 represents C_{1-10} alkyl substituted with one R^{13} group, and R^{13} represents halo, R^1, R^2, R^5 and R^6 do not represent C_{1-3}alkyl;

R^4 is selected from the group consisting of: C_{3-10} alkyl, C_{3-7} cycloalkyl, Aryl, HAR, Hetcy, $C(O)C_{5-10}$ alkyl, $C(O)C_{3-7}$ cycloalkyl, C(O)-Aryl, C(O)-HAR, C(O)-Hetcy, $CONR^9R^{10}$, CO_2R^9 and SO_2R^9, the alkyl, cycloalkyl, Aryl, HAR and Hetcy groups and portions being optionally substituted with 1-4 substituents selected from R^{13};

one of $R^5$and R^6 is selected from the group consisting of $NR^{11}R^{12}$, $NR^{11}COR^{12}$, $NR^{11}CO_2R^{12}$ and $NR^{11}S(O)_2R^{12}$, and the other represents R^1, HAR, Hetcy or OR^{11}, said HAR

and Hetcy being optionally substituted with 1-4 substituents selected from R^{13},

R^7, R^{10} and R^{11} are selected from the group consisting of: R^1 as defined above, HAR and Hetcy, said HAR and Hetcy being optionally substituted with 1-4 substituents selected from R^{13};

R^8, R^9 and R^{12} are selected from the group consisting of: C_{1-10}alkyl, C_{3-7}cycloalkyl, Aryl, HAR and Hetcy, said alkyl, cycloalkyl, Aryl, HAR and Hetcy being optionally substituted with 1-4 substituents selected from R^{13};

or alternatively, R^7, R^8, R^9 and R^{10} are as defined above, and R^{11} and R^{12} are taken together with the atoms to which they are attached along with any intervening atoms and represent a 5-8 membered ring optionally containing 1-2 heteroatoms selected from O, S and N, and optionally substituted with 1-4 substituents selected from R^{13};

each R^{13} is selected from the group consisting of: halo, $NR^{14}R^{15}$, C_{1-4}alkyl, C_{3-7}cycloalkyl, Aryl, HAR, Hetcy, CF_3, OCF_3, OR^{15}, NO_2, $S(O)_xR^{14}$, SR^{14}, $S(O)_xNR^{14}R^{15}$, $O(CR^{16}R^{17})_yNR^{14}R^{15}$, $C(O)R^{14}$, CO_2R^{15}, $CO_2(CR^{16}R^{17})_yCONR^{14}R^{15}$, $OC(O)R^{14}$, CN, $C(O)NR^{14}R^{15}$, $NR^{15}C(O)R^{14}$, $NR^{15}C(O)OR^{14}$, $NR^{15}C(O)NR^{16}R^{14}$ and CR^{15}(N-OR^{14}), wherein x is 1 or 2, and y is an integer from 1-4,

said alkyl, cycloalkyl, Aryl, HAR and Hetcy being optionally substituted with 1-4 substituents selected from R^{18};

R^{14}, R^{15}, R^{16} and R^{17} are independently selected from the group consisting of: H, C_{1-10}alkyl, C_{3-7}cycloalkyl, Aryl and Ar-C_{1-10}alkyl;

and each R^{18} is independently selected from the group consisting of: halogen, CN, C_{1-4}alkyl, OH, CF_3, Aryl, Aryloxy, CO_2H and CO_2C_{1-4} alkyl, said Aryl and the Aryl portion of Aryloxy being optionally substituted with up to 4 halo groups, and up to 2 C_{1-4} alkyl, OH, CF_3 or CN groups.

2. (Original) A compound in accordance with claim 1 wherein R^1 is selected from the group consisting of: H, C_{1-10}alkyl, C_{3-6} cycloalkyl and phenyl, said alkyl and phenyl being optionally substituted with 1-3 substituents selected from R^{13}.

3. (Original) A compound in accordance with claim 1 wherein R^2 is H.

4. ~~A compound in accordance with claim 1 wherein m is 0 and n is 2 or 3, or m is 1 and n is 1 or 2, such that the sum of m and n is 2 or 3.~~

5. (Original) A compound in accordance with claim 1 wherein R^3 is C_{3-10} alkyl optionally substituted with 1-4 substituents selected from R^{13}, such that when R^3 is substituted with one R^{13} group, and R^{13} represents halo, R^1, R^2, R^5 and R^6 do not represent C_{1-3}alkyl.

6. (Original) A compound in accordance with claim 5 wherein R^3 represents C_{3-5} alkyl, optionally substituted with 1-4 R^{13} groups.

7. (Original) A compound in accordance with claim 1 wherein R^4 is selected from the group consisting of: C_{5-10} alkyl, C_{3-6} cycloalkyl, phenyl, HAR, Hetcy, $C(O)C_{5-10}$alkyl, $C(O)C_{3-6}$ cycloalkyl and CO_2R^9, the alkyl, cycloalkyl and, Aryl groups and portions, phenyl, HAR and Hetcy being optionally substituted with 1-4 substituents selected from R^{13}, and R^9 representing C_{1-10}alkyl, C_{3-7}cycloalkyl, Aryl, HAR or Hetcy, said alkyl, cycloalkyl, Aryl groups and portions, HAR and Hetcy being optionally substituted with 1-4 R^{13} groups.

8. ~~A compound in accordance with claim 1 wherein X represents CR^5R^6, R^5 is $NR^{11}R^{12}$, and R6 is selected from the group consisting of: R^+, HAR, Hetcy and OR^{11}; wherein R^+ is as originally defined, R^{11} is R^+ or HAR, and R^{12} is C_{1-6} alkyl, Aryl or HAR, said Aryl and HAR being optionally substituted with 1-4 R^{13} groups,~~

~~or R^{11} and R^{12} are taken in combination with the atom to which they are attached and represent a 5-6 membered ring optionally substituted with 1-2 R^{13} groups.~~

9. (Original) A compound in accordance with claim 1 wherein R^{13} is selected from the group consisting of: halo, C_{1-4}alkyl, C_{3-7}cycloalkyl, Aryl, HAR, Hetcy, and OR^{15} wherein R^{15} is H,

said alkyl, cycloalkyl, Aryl, HAR and Hetcy being optionally substituted with 1-4 substituents selected from R^{18} and

R^{18} is halo, C_{1-4}alkyl, Aryl or CO_2C_{1-4} alkyl.

10. ~~A compound in accordance with claim 1 wherein:~~

~~R^+ is selected from the group consisting of: H, C_{1-10}alkyl, C_{3-6} cycloalkyl and~~

~~phenyl, said alkyl and phenyl being optionally substituted with 1-3 substituents selected from R^{13};~~

~~R^2 is H;~~

~~m is 0 and n is 2 or 3, or m is 1 and n is 1 or 2, such that the sum of m and n is 2 or 3;~~

~~R^3 is C_{3-10} alkyl optionally substituted with 1-4 substituents selected from R^{13}; such that when R^3 is substituted with one R^{13} group, and R^{13} represents halo, R^1, R^2, R^5 and R^6 do not represent C_{1-3} alkyl;~~

~~R^4 is selected from the group consisting of: C_{5-10} alkyl, C_{3-6} cycloalkyl, phenyl, HAR, Hetcy, $C(O)C_{5-10}$ alkyl, $C(O)C_{3-6}$ cycloalkyl and CO_2R^9, the alkyl, cycloalkyl and, Aryl groups and portions, phenyl, HAR and Hetcy being optionally substituted with 1-4 substituents selected from R^{13}, and R^9 representing C_{1-10} alkyl, C_{3-7} cycloalkyl, Aryl, HAR or Hetcy, said alkyl, cycloalkyl, Aryl groups and portions, HAR and Hetcy being optionally substituted with 1-4 R^{13} groups;~~

~~X represents CR^5R^6, R^5 is $NR^{11}R^{12}$, and R6 is selected from the group consisting of: R^1, HAR, Hetcy and OR^{11}, wherein R^1 is as originally defined, R^{11} is R^1 or HAR, and R^{12} is C_{1-6} alkyl, Aryl or HAR, said Aryl and HAR being optionally substituted with 1-4 R^{13} groups;~~

~~or R^{11} and R^{12} are taken in combination with the atom to which they are attached and represent a 5-6-membered ring optionally substituted with 1-2 R^{13} groups;~~

~~R^{13} is selected from the group consisting of: halo, C_{1-4} alkyl, C_{3-7} cycloalkyl, Aryl, HAR, Hetcy, and OR^{15} wherein R^{15} is H;~~

~~said alkyl, cycloalkyl, Aryl, HAR and Hetcy being optionally substituted with 1-4 substituents selected from R^{18} and~~

~~R^{18} is halo, C_{1-4} alkyl, Aryl or CO_2C_{1-4} alkyl.~~

11. (Amended) A compound in accordance with claim 1 selected from the group consisting of:

tert-butyl 3-cyano-2-[(2-ethylbutanoyl)amino]-5,6-dihydrothieno[2,3-b]pyridine-7(4H)-carboxylate;

N-(3-cyano-7-isobutyl-4,5,6,7-tetrahydrothieno[2,3-b]pyridin-2-yl)-2-ethylbutanamide; and

N-(3-cyano-7-isopropyl-4,5,6,7-tetrahydrothieno[2,3-b]pyridin-2-yl)-2-ethylbutanamide.;

~~N-{6-[(4'-chloro-1,1'-biphenyl-4-yl)methyl]-3-cyano-4,5,6,7-tetrahydrothieno[2,3-c]pyridin-2-yl}-2-ethylbutanamide;~~

~~N-[3-cyano-6-(4-phenoxybenzyl)-4,5,6,7-tetrahydrothieno[2,3-c]pyridin-2-yl]-2-ethylbutanamide;~~

~~N-{6-[4-(4-chlorophenoxy)benzyl]-3-cyano-4,5,6,7-tetrahydrothieno[2,3-c]pyridin-2-yl}-2-ethylbutanamide;~~
~~N-[3-cyano-6-(3-phenoxybenzyl)-4,5,6,7-tetrahydrothieno[2,3-c]pyridin-2-yl]-2-ethylbutanamide;~~
~~N-(3-cyano-6-{[1-(2,4-dichlorophenyl)cyclopropyl]carbonyl}-4,5,6,7-tetrahydrothieno[2,3-c]pyridin-2-yl)-2-ethylbutanamide;~~
~~N-{3-cyano-6-[(2,4-dichlorobenzyl)amino]-4,5,6,7-tetrahydro-1-benzothien-2-yl}-2-ethylbutanamide;~~
~~N-{3-cyano-6-[(cyclopropylmethyl)(2,4-dichlorobenzyl)amino]-4,5,6,7-tetrahydro-1-benzothien-2-yl}-2-ethylbutanamide;~~
~~N-{3-cyano-6-[(2,4-dichlorobenzyl)(isopropyl)amino]-4,5,6,7-tetrahydro-1-benzothien-2-yl}-2-ethylbutanamide;~~
~~N-{3-cyano-6-[(2,4-dichlorobenzyl)(isopentyl)amino]-4,5,6,7-tetrahydro-1-benzothien-2-yl}-2-ethylbutanamide;~~
~~N-{3-cyano-6-[(2,4-dichlorobenzyl)(3,3-dimethylbutyl)amino]-4,5,6,7-tetrahydro-1-benzothien-2-yl}-2-ethylbutanamide;~~
~~N-{3-cyano-6-[(2,4-dichlorobenzyl)(isobutyl)amino]-4,5,6,7-tetrahydro-1-benzothien-2-yl}-2-ethylbutanamide;~~
~~N-{3-cyano-6-[(2,4-dichlorobenzyl)(2-ethylbutyl)amino]-4,5,6,7-tetrahydro-1-benzothien-2-yl}-2-ethylbutanamide;~~
~~N-(3-cyano-6-{(2,4-dichlorobenzyl)[(4,5-dimethyl-2-furyl)methyl]amino}-4,5,6,7-tetrahydro-1-benzothien-2-yl)-2-ethylbutanamide;~~
~~N-{3-cyano-6-[(2,4-dichlorobenzyl)(3-phenylpropyl)amino]-4,5,6,7-tetrahydro-1-benzothien-2-yl}-2-ethylbutanamide;~~
~~N-{6-[(1-benzofuran-2-ylmethyl)(2,4-dichlorobenzyl)amino]-3-cyano-4,5,6,7-tetrahydro-1-benzothien-2-yl}-2-ethylbutanamide;~~
~~N-{3-cyano-6-[(2,4-dichlorobenzyl)(3,3,3-trifluoropropyl)amino]-4,5,6,7-tetrahydro-1-benzothien-2-yl}-2-ethylbutanamide;~~
~~N-{3-cyano-6-[(2,4-dichlorobenzyl)(4-fluorobenzyl)amino]-4,5,6,7-tetrahydro-1-benzothien-2-yl}-2-ethylbutanamide;~~
~~N-{3-cyano-6-[(2,4-dichlorobenzyl)(tetrahydrofuran-2-ylmethyl)amino]-4,5,6,7-tetrahydro-1-benzothien-2-yl}-2-ethylbutanamide;~~
~~N-(3-cyano-6-{(2,4-dichlorobenzyl)[(5-methyl-2-furyl)methyl]amino}-4,5,6,7-tetrahydro-1-benzothien-2-yl)-2-ethylbutanamide;~~

~~tert-butyl (2S)-2-{[{3-cyano-2-[(2-ethylbutanoyl)amino]-4,5,6,7-tetrahydro-1-benzothien-6-yl}(2,4-dichlorobenzyl)amino]methyl}pyrrolidine-1-carboxylate;~~

~~N-{3-cyano-6-[(3,4-dichlorobenzyl)amino]-4,5,6,7-tetrahydro-1-benzothien-2-yl}-2-ethylbutanamide;~~

~~N-{3-cyano-6-[(3,4-dichlorobenzyl)(methyl)amino]-4,5,6,7-tetrahydro-1-benzothien-2-yl}-2-ethylbutanamide;~~

~~N-(3-cyano-6-{[(2-phenyl-1,3-thiazol-5-yl)methyl]amino}-4,5,6,7-tetrahydro-1-benzothien-2-yl)-2-ethylbutanamide;~~

~~N-(3-cyano-6-{methyl[(2-phenyl-1,3-thiazol-5-yl)methyl]amino}-4,5,6,7-tetrahydro-1-benzothien-2-yl)-2-ethylbutanamide;~~

~~N-(3-cyano-6-{[(2-phenyl-1,3-thiazol-4-yl)methyl]amino}-4,5,6,7-tetrahydro-1-benzothien-2-yl)-2-ethylbutanamide;~~

~~N-(3-cyano-6-{methyl[(2-phenyl-1,3-thiazol-4-yl)methyl]amino}-4,5,6,7-tetrahydro-1-benzothien-2-yl)-2-ethylbutanamide;~~

~~N-[3-cyano-6-(1,2,3,4-tetrahydronaphthalen-1-ylamino)-4,5,6,7-tetrahydro-1-benzothien-2-yl]-2-ethylbutanamide;~~

~~N-{3-cyano-6-[methyl(1,2,3,4-tetrahydronaphthalen-1-yl)amino]-4,5,6,7-tetrahydro-1-benzothien-2-yl}-2-ethylbutanamide;~~

~~N-{3-cyano-6-[(2,3-dihydro-1H-inden-1-ylmethyl)amino]-4,5,6,7-tetrahydro-1-benzothien-2-yl}-2-ethylbutanamide;~~

~~N-{3-cyano-6-[(2,3-dihydro-1H-inden-1-ylmethyl)(methyl)amino]-4,5,6,7-tetrahydro-1-benzothien-2-yl}-2-ethylbutanamide;~~

~~N-{6-[(2-chlorobenzyl)amino]-3-cyano-4,5,6,7-tetrahydro-1-benzothien-2-yl}-2-ethylbutanamide~~

~~N-{6-[(2-chlorobenzyl)(methyl)amino]-3-cyano-4,5,6,7-tetrahydro-1-benzothien-2-yl}-2-ethylbutanamide;~~

~~N-(6-{[1-(4-bromophenyl)ethyl]amino}-3-cyano-4,5,6,7-tetrahydro-1-benzothien-2-yl)-2-ethylbutanamide;~~

~~N-{6-[[1-(4-bromophenyl)ethyl](methyl)amino]-3-cyano-4,5,6,7-tetrahydro-1-benzothien-2-yl}-2-ethylbutanamide;~~

~~N-[3-cyano-6-(3-phenylpyrrolidin-1-yl)-4,5,6,7-tetrahydro-1-benzothien-2-yl]-2-ethylbutanamide;~~

~~N-[3-cyano-6-(4-phenylpiperazin-1-yl)-4,5,6,7-tetrahydro-1-benzothien-2-yl]-2-ethylbutanamide;~~

~~N-{3-cyano-2-[(2-ethylbutanoyl)amino]-4,5,6,7-tetrahydro-1-benzothien-6-yl}-N-(2,4-dichlorobenzyl)-3,3-dimethylbutanamide;~~

~~N-{3-cyano-2-[(2-ethylbutanoyl)amino]-4,5,6,7-tetrahydro-1-benzothien-6-yl}-N-[1-(hydroxymethyl)-2,2-dimethylpropyl]cyclopropanecarboxamide;~~

~~N-{3-cyano-2-[(2-ethylbutanoyl)amino]-4,5,6,7-tetrahydro-1-benzothien-6-yl}-N-[1-(hydroxymethyl)-2,2-dimethylpropyl]-3,3-dimethylbutanamide;~~

~~N-{3-cyano-2-[(2-ethylbutanoyl)amino]-4,5,6,7-tetrahydro-1-benzothien-6-yl}-N-[1-(hydroxymethyl)-2,2-dimethylpropyl]cyclopentanecarboxamide;~~

~~N-{3-cyano-2-[(2-ethylbutanoyl)amino]-4,5,6,7-tetrahydro-1-benzothien-6-yl}-N-[1-(hydroxymethyl)-2,2-dimethylpropyl]benzamide and~~

~~N-{3-cyano-2-[(2-ethylbutanoyl)amino]-4,5,6,7-tetrahydro-1-benzothien-6-yl}-N-[1-(hydroxymethyl)-2,2-dimethylpropyl]cyclohexanecarboxamide.~~

12. (Original) A pharmaceutical composition which is comprised of a compound in accordance with claim 1 in combination with a pharmaceutically acceptable carrier.

13. (Original) A method of treating type 2 diabetes mellitus in a mammalian patient in need of such treatment, comprising administering to said patient a compound in accordance with claim 1 in an amount that is effective to treat type 2 diabetes mellitus.

14. ~~A method of preventing or delaying the onset of type 2 diabetes mellitus in a mammalian patient in need thereof, comprising administering to said patient a compound in accordance with claim 1 in an amount that is effective to prevent or delay the onset of type 2 diabetes mellitus.~~

15. ~~A method of treating, preventing or delaying the onset of a disease or condition in a type 2 diabetes mellitus patient, said disease or condition being selected from the group consisting of: dyslipidemia selected from elevated serum cholesterol, elevated serum triglycerides, elevated serum low-density lipoproteins and low levels of serum high-density lipoprotein, microvascular or macrovascular changes and the sequellae of such conditions selected from coronary heart disease, stroke, peripheral vascular disease, hypertension, renal hypertension, nephropathy, neuropathy and retinopathy, said method comprising administering to the type 2 diabetic patient an amount of a compound of formula I that is effective for treating, preventing or delaying the onset of such diseases or conditions.~~